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Regional differences in albuminuria among American Indians: An epidemic of renal disease

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Regional differences in albuminuria among American Indians: An epidemic of renal disease. Albuminuria is a risk factor for renal and cardiovascular disease. We conducted a cross sectional survey of 4549 older American Indians in Arizona, Oklahoma and North and South Dakota of (micro)albuminuria. A range of 20.1 to 48.3% of all participants had either micro- ($\geq$ 30 to $<$ 300 mg albumin/g creatinine) or macroalbuminuria ($\geq$ 300 mg albumin/g creatinine). A total of 53% of the participants were diabetic, and the prevalence in Arizona (65 to 70%) was significantly greater than the other two sites. Prevalence of micro- and macroalbuminuria were significantly higher among those who were older, diabetic or hypertensive, and participants from Arizona. Even normotensive, nondiabetic Arizona Indians had higher prevalence rates than similar participants elsewhere. Higher prevalence rates of micro- and macroalbuminuria were also found among Arizona participants than participants with similar degrees of glucose intolerance from the other two sites. Indians reporting the greatest degree of Indian blood were more likely to have abnormal albuminuria ($P < 0.0001$). The duration of diabetes, fasting plasma glucose, systolic blood pressure, fibrinogen and Indian heritage were independently associated with micro- or macroalbuminuria. The association of albuminuria with subsequent ESRD, cardiovascular morbidity and overall mortality suggests that these American Indians will face a large disease burden. The correlation with reported Indian blood implies a strong component of genetic susceptibility, possibly independent of diabetes.

Increased concentration of albumin in the urine of diabetic individuals is a strong and independent predictor of all-cause and coronary heart disease mortality [1, 2]. In comparison to a type 1 (insulin dependent) diabetic cohort whose urine contained normal amounts of albumin, patients with microalbuminuria faced nearly a 200-fold increased risk of cardiovascular disease in the decade following the initial observation [3, 4]. These findings led to speculation that the albumin "leak" in the glomeruli reflects a widespread capillary vasculopathy affecting the heart, eyes, and perhaps other organs [5, 6]. The appearance of nephropathy may not be a simple consequence of diabetes. Family studies indicate that diabetic nephropathy is more likely to occur among children of parents with nephropathy, families with hypertension, or in siblings of patients with nephropathy [7–10]. Furthermore, the presence of small, but abnormal amounts of albumin in the urine is predictive of progression to overt nephropathy [11]. Thus, measurements of albumin concentrations by sensitive techniques are a valuable clinical, epidemiologic and public health tool.

The Strong Heart Study was begun in 1988 to measure risk factors and cardiovascular disease among diverse groups of American Indians. The examination included an interview, physical examination, collection of blood and urine, and a two-hour glucose tolerance test. In light of the evolving importance of albuminuria, sensitive measurements of urine albumin and creatinine were included in the phase-I examination. The expectation was that the prevalence of albuminuria would be high, since previous studies of certain American Indian populations reported high rates of proteinuria [12, 13] and end-stage renal disease [14–16]. In this paper, we summarize the prevalence rates of albuminuria and its relation to other risk factors, and show data indicating significant differences in the rates of albuminuria among the three centers of the study.

Methods

Details summarizing design of this study [17], observed cardiovascular risk factors [18, 19] and prevalence of diabetes [20] among the 4549 eligible participants are summarized in recent publications. The Strong Heart Study population consisted of 4549 American Indians aged 45 to 74 years old living in Oklahoma, South and North Dakota and Arizona. The examinations occurred between July 1, 1989 and January 31, 1992. Percent participation rates of the target population were 71% in Arizona, 53% in North and South Dakota and 62% in Oklahoma. The participation rates were calculated using the total number of persons in the December, 1988 tribal lists. Non-respondents did not differ significantly from respondents in age, body mass index, and self-reported incidence of diabetes or hypertension. A slightly higher proportion of respondents were women compared to non-respondents, and a higher proportion of the non-responders were smokers.

Participants were members of the following tribes: Pima, Maricopa and Tohono O'odham of central Arizona living in the Gila River, Salt River and Ak-Chin Indian Communities; seven tribes

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Table 1. Prevalence of diabetes by age and site

		Arizona		Oklahoma		Dakotas	
Age	Sex	*N* of subjects	Prevalence %	*N* of subjects	Prevalence %	*N* of subjects	Prevalence %
45–54	M	281	62.3	289	29.8	282	29.4
	F	423	65.0	327	28.8	356	33.4
55–64	M	326	71.3	200	40.5	212	36.3
	F	157	76.1	304	47.7	287	47.7
65–74	M	175	60.2	126	46.0	111	32.4
	F	83	75.4	197	50.3	159	56.0
Total		1445	68.7	1443	39.0	1407	38.5

of Southwestern Oklahoma (Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita); and the Oglala and Cheyenne River Sioux in South Dakota and the Devils Lake Sioux in the Fort Totten area of North Dakota. The study received approval of the Institutional Review Boards of the participating institutions and Indian communities.

Briefly, the standardized clinical examination took place after a twelve hour overnight fast. It consisted of a personal interview, a physical examination including a 12-lead electrocardiogram, and a review of current medications. A 75 gram oral glucose tolerance test (OGTT; Glutol, Paddock Laboratory, Inc., Minneapolis, MN, USA) was performed, and blood was obtained two hours later to measure plasma glucose. Participants were excluded from the OGTT if their fasting capillary glucose was ≥225 mg/dl (AccuChek-II, Baxter Health Care Corp., Grand Prairie, TX, USA), or if previously diagnosed as having diabetes and currently using an oral agent or insulin. Additionally, a small number of participants who had chronic renal failure were excluded from the glucose tolerance test. Participants were considered as having diabetes if they were taking insulin or an oral hypoglycemic medication, or if their fasting plasma glucose ≥ 140 mg/dl or their two-hour plasma glucose ≥ 200 mg/dl [21]. Participants were considered having impaired glucose tolerance if their fasting plasma < 140 mg/dl and the two hours plasma glucose value ≥ 140 and < 200 mg/dl.

A random urine specimen was obtained on arrival to the clinic (usually between 0800 and 0900 hr) for measurement of creatinine and albumin content. Fasting blood was obtained for measurement of plasma lipids and apolipoproteins, plasma glucose and fibrinogen [22]. Each laboratory measurement was performed in a central laboratory using stable methodology standardized to outside reference values. Serum and urine creatinine were measured by the picric acid method [23]. Plasma glucose was measured on the Hitachi 704, 705 or 717 autoanalyzer using a hexokinase method (Boerhinger Mannheim/HK) standardized to controls provided by the manufacturer (PreciCal, PreciNorm, PreciAbnorm) and the College of American Pathologists. Urine albumin content was measured by a sensitive, nephelometric technique [24]. Five percent of samples were duplicates sent to the reference laboratories as blinded samples for quality control purposes. Microalbuminuria was defined as albumin/creatinine ratios ≥ 30 and < 300 mg albumin/g creatinine. Macroalbuminuria was recognized as albumin concentrations ≥ 300 mg/g creatinine. Insulin was measured using antibody 1012, WHO-traceable (1988) insulin standards and supplies purchased from Linco Research, Inc. (St. Louis, MO, USA). The interassay and intra-assay coefficients of variation of the insulin assay at midrange were 8.5% and 2.2%, respectively. Technical errors (coefficient of variation between blinded pairs) for the plasma measurements were as follows: cholesterol 5.8%, triglycerides 10.2%, fibrinogen 12.4%, urine creatinine 8.7%, urine albumin 6.4% and fasting plasma glucose 13.6%.

Height and weight were measured with the participant in light clothing with shoes removed. Waist circumference was obtained at the umbilicus with the participant in the supine position. Hip circumference was measured over light clothing while the participant was standing: the greatest diameter around the buttocks was recorded. Electrical impedance was estimated by use of an RJL Impedance Meter (Model B14101, RJL Equipment Co., Detroit, MI, USA) and percent body fat was calculated using the Segal formula [25]. Blood pressure measurements (Baum Sphygmomanometer Co. Copiaque, NY, USA) were obtained according to A.H.A. standardized protocol in the right arm with the participant in the sitting position, and after five minutes of rest. Participants were considered to have definite hypertension if they had a systolic BP ≥ 140 mm Hg, or a diastolic BP ≥ 90 mm Hg, or if they were taking antihypertensive medication. Indian heritage was expressed as percent of Indian blood and based on self-reported data obtained during the interview. Normal, overweight and obesity were classified on the basis of body mass index [26].

Significance of center-specific differences was evaluated by analysis of variance. Univariate analyses were first performed to describe albuminuria. Analysis of variance and multiple comparison of means were used to compare the differences among subgroups. The chi-square test was used to compare the prevalence rates. Ninety-five percent confidence intervals were constructed for means of continuous variables. Stepwise logistic regression was employed to simultaneously adjust the covariates and determine their relative significance.

Results

A detailed description of the characteristics of the study population is published elsewhere [18]. Briefly, fifty percent of the participants were from the lower decade of age, 45 to 54 years. The mean (SD) ages were 55.7 (7.9) in Arizona, 56.8 (8.3) in Oklahoma and 56.5 (8.0) in North/South Dakota. Approximately equal numbers of participants (1500 in Arizona, 1527 in Oklahoma, 1522 in North/South Dakota) were studied at each site, but there was a slight preponderance (59%) of women at all sites.

A strikingly large proportion of the examinees were diabetic, and the distribution of diabetes by age, sex and site is shown in Table 1. Among the total study population 53% were classified as diabetic on the basis of known diabetes or a diabetic glucose tolerance test. The greatest prevalence, by far, was detected in Arizona ($P < 0.0001$). In each site, the prevalence rates for women were higher than for men, and the gender difference was significant at all study sites.

There were some small but highly significant differences in mean blood pressure at the three sites (Table 2). Mean systolic blood pressure (SBP) and and diastolic blood pressure (DBP) were higher in Arizona and Oklahoma than in the Dakotas in both male and female participants ($P < 0.0001$). The prevalence of hypertension was 42 to 47% in Arizona and Oklahoma, but only about 27% in participants from the Dakotas ($P < 0.01$).

Table 2 also shows the mean BMIs and percent body fat for the study populations. In general, the study populations were obese,

Table 2. Mean blood pressure, hypertension and obesity by site

	Arizona		Oklahoma		Dakotas	
	Men	Women	Men	Women	Men	Women
Mean systolic BP *mm Hg*	131	132	131	129	124	122
Hypertension %[a]	44.2	42.5	46.7	42.3	27.2	27.6
Mean BMI	31.1	33.1	30.2	31.3	28.5	30.1
Mean % body fat	32.8	44.1	32.4	43.3	31.1	42.4
Mean WHR	0.97	0.96	0.96	0.93	0.98	0.94

[a] By JNC-V criteria; SBP > 140, dBP > 90 or taking antihypertensive medications

Table 3. Prevalence rates of albuminuria by age and site

	DM			IGT			NGT		
	nl	micro	macro	nl	micro	macro	nl	micro	macro
Arizona *total 1411*									
N	346	331	283	160	29	15	202	36	9
45–54	38.7	36.0	25.3	81.5	13.0	5.6	79.6	16.2	4.2
55–64	35.0	33.1	31.9	80.7	10.5	8.8	88.7	9.4	1.9
65–74	34.3	38.6	27.1	66.7	23.1	10.3	82.1	14.3	3.6
Oklahoma *total 1416*									
N	323	148	76	216	26	5	576	40	6
45–54	61.8	27.5	10.6	90.3	9.7	0.0	93.7	5.1	1.2
55–64	57.4	25.8	16.8	92.5	3.0	4.5	95.1	3.9	1.0
65–74	57.3	29.0	13.8	75.9	20.7	3.5	82.6	17.4	0.0
Dakotas *total 1472*									
N	303	135	78	210	20	5	675	41	5
45–54	57.6	29.4	12.8	92.4	7.6	0.0	92.7	6.6	0.6
55–64	64.1	20.2	15.7	88.3	5.2	6.5	92.8	6.2	1.0
65–74	50.9	30.6	18.5	82.9	17.1	0.0	90.5	8.3	1.2

Table 4. Prevalence (%) of abnormal albuminuria

	Arizona		Oklahoma		Dakotas	
	micro	macro	micro	macro	micro	macro
All participants						
Prevalence of abnormal albuminuria	28.3	20.0	15.2	6.1	13.8	6.3
Diabetic participants only						
Duration of DM *years*						
0–4	32.2	8.2	18.4	7.1	22.0	6.0
5–9	44.7	20.0	30.2	11.5	35.8	14.7
10–14	34.6	25.4	39.8	15.9	25.0	23.5
>15	33.8	47.9	32.7	30.0	29.3	41.3
Fasting PI. glucose *mg/dl*						
<110	21.6	37.3	10.6	10.6	21.6	11.8
111–139	27.0	19.2	18.7	11.4	13.9	9.9
>139	37.9	29.1	31.8	15.0	30.3	17.4
Hypertension						
No	37.3	18.8	23.1	8.4	25.2	9.4
Yes	33.3	38.0	30.4	17.7	27.5	25.3
Body mass index[a]						
Normal	37.5	36.1	28.7	16.7	29.2	16.2
Overweight	34.9	33.1	25.7	12.5	27.0	13.8
Obese	34.3	20.1	27.4	13.2	23.6	15.6
Fibrinogen						
Lower 1/3	30.5	12.4	28.1	8.5	24.6	8.6
Middle 1/3	46.3	18.5	26.8	7.7	28.1	14.4
Top 1/3	30.0	43.5	26.0	28.6	26.7	31.4

[a] Body mass index categories

	Normal	Overweight	Obese
men	<27.8	27.8–31.0	>31.1
women	<27.3	27.3–32.2	>32.3

and the fat distribution was predominantly in the upper body. Participants in Arizona had significantly ($P < 0.0001$) higher BMIs and percentages of body fat than those at the other two sites.

Table 3 summarizes the prevalence of normal, micro- and macroalbuminuria within each site by age. Data were available from slightly more than 1400 participants from each site. Among the categories shown, about 35 to 65% of those with diabetes had either micro- or macroalbuminuria. Several trends were evident. Abnormal albuminuria was most prevalent among those with diabetes. Those with impaired glucose tolerance generally had higher rates than those with normal glucose tolerance. In addition, the prevalence rates of abnormal albuminuria in almost every category were higher in Arizona than in the other two sites.

Table 4 summarizes the prevalence of abnormal albuminuria among diabetic participants by duration of diabetes, fasting plasma glucose, hypertension, body mass index and plasma fibrinogen concentrations. The overall prevalence rates among the participants are displayed in the first row. The distribution of albuminuria was associated with each of these variables, but within categories of each of them, the distribution of abnormal albuminuria was shifted toward higher values in the Arizona sites ($P < 0.001$ for association with site, stratified by each of the other variables shown in the table, by the Mantel-Haenszel test). For example, even among those who were normotensive, non-obese or nondiabetic, rates of micro- and macroalbuminuria were highest among participants in Arizona. Further evidence for the higher rates of albuminuria in Arizona is found in Table 5 where medians of albumin/creatinine ratios among the participants are shown by site, and stratified within categories of variables thought to be associated with albuminuria. Median albumin/creatinine ratios were higher among Arizona participants for each of the categories; median albumin/creatinine ratios were highest in Arizona even among the youngest (45 to 54 years of age), normotensive and those with the lowest levels of glycemia. Figure 1 shows the relative frequencies of albuminuria among the three sites stratified by glucose tolerance. In each glucose tolerance category, higher ratios of urinary albumin/creatinine values were more common among participants in Arizona than in the other two sites. Conversely, normal ratios of albumin/creatinine were less common among participants from Arizona within each of the glucose tolerance categories.

Figure 2 shows the prevalence of albuminuria by Indian heritage. Those with greater percentages of Indian blood also had the highest prevalence of albuminuria (micro + macro). This trend is especially evident in the Dakotas and Oklahoma where non-Indian admixture was more common. The trend was least evident in Arizona where non-Indian admixture was quite uncommon. In Arizona, less than 10% of the participants reported that they were not full-blooded Indians. The significance of the trend was tested with the Cochran-Armitage test of the hypothesis that the prevalence is not linearly related to the degree of Indian heritage. Quartile scores of reported heritage were assumed to be equally spaced categories. Within each site, Indian heritage was significantly associated with albuminuria ($P < 0.05$) among

Table 5. Median albumin/creatinine ratio (mg/g) by age, SBP, FPG in all participants and duration of DM in diabetic participants only

	Arizona	Oklahoma	Dakotas
Age			
45–54	22.3	7.5	6.3
55–64	33.3	8.4	7.7
≥65	33.8	13.3	12.1
SBP			
≤140	18.7	7.3	6.7
140–159	62.7	14.1	11.8
≥160	311.2	31	76.3
FPG			
≤110	10.1	6.5	5.4
111–139	13.8	7.3	7.5
≥140	71.2	24.9	27.7
DM duration			
0–4	19.9	11.8	13.2
5–10	56.2	23.1	26.8
10–15	69.9	39.3	46.8
≥15	294.7	92.1	123.4

those with diabetes. Among those with IGT or normal glucose tolerance, the association was significant only in Oklahoma (P = 0.01).

The prevalence odds ratios comparing the participants in the upper quartiles to those in the lower quartiles of several variables associated with albuminuria is summarized in Table 6. In this analysis, it can be seen that those with higher blood sugars, blood pressure and fibrinogen concentrations were at increased risk for micro- or macroalbuminuria. In addition, men and those from Arizona were more likely to have abnormal albuminuria. Interestingly, neither hyperinsulinemia nor waist-hip ratio were significantly associated with albuminuria in this model. The duration of diabetes, fasting plasma glucose, systolic blood pressure and fibrinogen were the four most powerful and consistent correlates of albuminuria.

Discussion

This cross sectional study demonstrates a high prevalence of abnormal albuminuria among these groups of older American Indians. Prevalence rates in Arizona were significantly different, with much higher rates of macroalbuminuria and microalbuminuria than the other two centers. Abnormal albuminuria was strongly associated with diabetes and systolic hypertension at all three sites, but albuminuria was clearly more common even among Arizona participants who were non-diabetic and normotensive than similar participants in the Dakotas or Oklahoma. Furthermore, macro- and microalbuminuria were significantly more common among participants who reported high degrees of Indian heritage.

The high prevalence of microalbuminuria and macroalbuminuria found among Strong Heart Study participants is consistent with earlier observations detecting high prevalence rates of end-stage renal disease and proteinuria among several Indian groups including the Pima-Papago tribes in Arizona. For example, Nelson and associates reported on the prevalence of albuminuria among 2728 participants studied between 1982 and 1988 in the Gila River Indian Community in Arizona [12]. The study cohort included participants as young as 15 years and the mean age was younger than that of the Strong Heart Study. Using the same assay methods and definitions of micro and macroalbuminuria as this

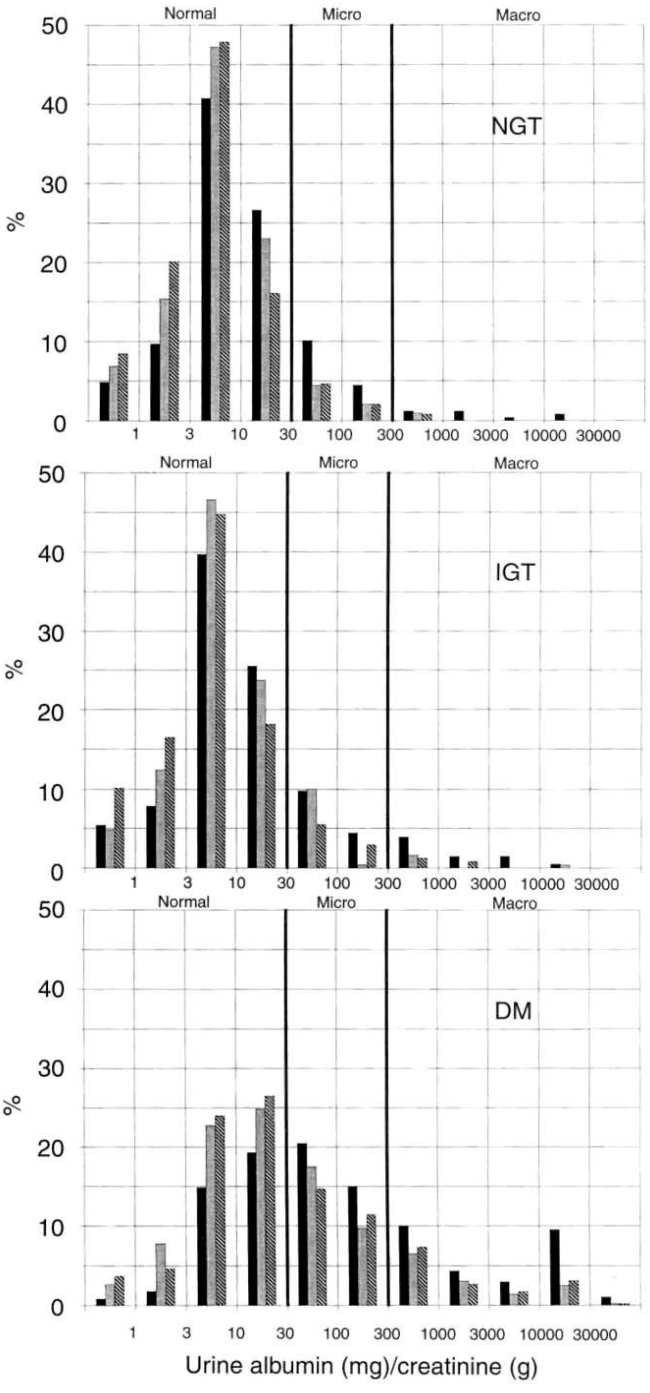

Fig. 1. *The relative frequencies of categories of albuminuria expressed by the ratio of urine albumin to creatinine concentrations found among the three study sites.* The uppermost, middle and lower panels summarize the distributions among the participants with normal (NGT), impaired (IGT) or diabetic (DM) glucose tolerance, respectively. Within each graph panel, separate vertical bars indicate the frequency within each of the three sites (■ Arizona; ▨ Oklahoma; (▧ South/North Dakota). The data show that participants with normal amounts of albumin in the urine are less frequent in Arizona than the other two sites. Conversely, micro- and macroalbuminuria are more commonly found among the Arizona Indians.

study, 13.1% of the subjects had microalbuminuria and 7.2% had macroalbuminuria. Nearly 8% of those with normal glucose tolerance had abnormal amounts of urine albumin. Nearly 47% of

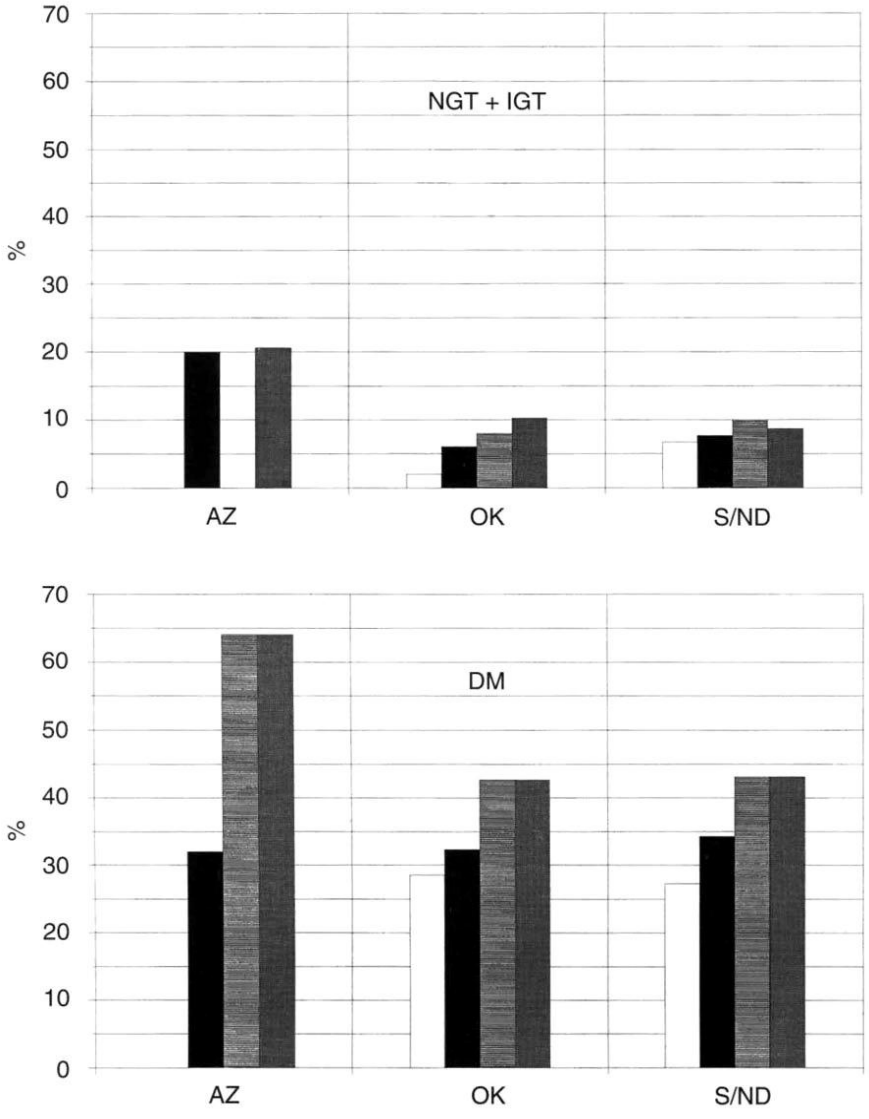

Fig. 2. *The prevalence of albuminuria is shown within each site according to quartile of reported Indian heritage.* Symbols are: (□) 0 to 49%; (■) 50 to 74%; (▤) 75 to 99%; (▦) 100%. Most participants in Arizona were full- or nearly full-blooded, and thus some categories had no reported participants (NGT + IGT: AZ 0 to 49% and 75 to 99%; DM: AZ 0 to 49%). Note that increasing amounts of reported Indian heritage was associated with a higher prevalence of albuminuria.

diabetic participants had some degree of abnormal albuminuria. Albuminuria was significantly associated with age, duration of diabetes, glycemia, blood pressure and insulin use.

While the Pima Indians may have the highest known prevalence of albuminuria, other Indian tribes also have higher prevalence rates of end-stage renal disease in comparison to whites, and the incidence appears to be increasing. The prevalence of end-stage renal disease among American Indians is a least 2.8 times that of the general population [14] and the incidence is said to be increasing at a rate of 17% per year [27]. The incidence among Pima Indians is 23 times that of the U.S. population [28].

The strong, independent association of albuminuria with plasma fibrinogen concentrations was anticipated; fibrinogen is thought to be an acute-phase reactant as part of the pathologic process of renal damage and vascular injury [29–31]. Our cross sectional data do not allow us to determine, with any confidence, if fibrinogen levels predict albuminuria. Follow-up studies, as part of phase II of the Strong Heart Study, are underway, and they will help determine the precise role, if any, for fibrinogen in producing susceptibility to abnormal albuminuria.

The association of Indian admixture with disease is complex. Although we found a close association of albuminuria with reported Indian heritage, there was no clear relationship of Indian Heritage to coronary heart disease prevalence in the same study population [19]. In contrast to cardiac disease, diabetes and impaired glucose tolerance were directly related to Indian heritage [20, 32].

We cannot, with the current data, determine if environmental factors account for some or possibly all of the site to site differences in renal dysfunction. Such factors as dietary sodium, protein and fat intake could not be reliably measured in phase I of the Strong Heart Study since only a limited number in each site underwent dietary assessment. A yet to be identified environmental toxin could also be hypothesized.

One of the most interesting aspects of this study is the detection of higher rates of macro- or microalbuminuria among nondiabetic

Table 6. Prevalence odds ratios of albuminuria derived from a multiple logistic regression analysis

	P	Q1 mean	Q4 mean	Odds ratio exp(beta*Q4-Q1)	Lower 95%	Upper 95%
Abnormal albuminuria (micro + MACRO *N* = 1274 vs. 2994 normal), all participants in all three centers						
Fasting plasma glucose	0.0001	92.0	262.9	7.915	6.541	9.578
SBP	0.0001	106.0	154.1	4.343	3.522	5.355
Age	0.0710	46.9	67.7	1.215	0.984	1.502
Plasma insulin	0.5859	6.5	44.3	1.038	0.908	1.187
Fibrinogen	0.0001	215.5	404.8	3.131	2.549	3.845
Indian Heritage	0.0001	0.0	34.5	1.393	1.186	1.636
WHR	0.2451	0.9	1.0	1.136	0.916	1.410
Arizona (1,0)	0.0001	0	1	1.802	1.518	2.139
Sex (F = 1, M = 0)	0.0113	0	1	0.803	0.678	0.952
Abnormal albuminuria (micro + MACRO *N* = 963 vs. 927 normal), diabetic participants only in all three centers						
Fasting plasma glucose	0.0001	92.0	262.9	3.568	2.774	4.589
SBP	0.0001	106.0	154.1	4.219	3.152	5.647
Age	0.0842	46.9	67.7	0.769	0.570	1.037
Plasma insulin	0.2570	6.5	44.3	0.916	0.786	1.067
Fibrinogen	0.0001	215.5	404.8	2.930	2.207	3.890
Indian Heritage	0.0190	0.0	34.5	1.333	1.048	1.694
WHR	0.5377	0.9	1.0	1.098	0.815	1.488
Arizona (1,0)	0.0192	0	1	1.314	1.045	1.652
Sex (F = 1, M = 0)	0.0008	0	1	0.677	0.539	0.851
DM duration	0.0001	0.1	23.3	4.402	3.227	6.005

and non-hypertensive participants in Arizona. Nelson and colleagues also found a high prevalence among non-diabetic Pima Indians in the Gila River Indian Community [12]. While the prevalence of abnormal albuminuria (micro- or macroalbuminuria) was higher in those with impaired glucose tolerance (15%) than in those with normal glucose tolerance (8%), the majority of cases among the nondiabetic subjects occurred in those with normal glucose tolerance and hence could not be attributed to clinically apparent hyperglycemia. Thus, additional explanations must be considered. For example, early renal disease may in some individuals be independent of diabetes. The later occurrence of diabetes, hypertension or introduction of certain environmental factors may then accelerate the renal damage and lead to progressive nephropathy. This hypothesis is supported by the observation in Pima Indians that blood pressure measured before the onset of diabetes predicted a greater prevalence of abnormal albuminuria after the onset of diabetes [33].

The potential public health implications of our observations are immense. In general, type I diabetic individuals with abnormal albuminuria have significantly increased risks of coronary heart disease [2, 4, 34], proliferative retinopathy [35], and accelerated progression to end-stage renal disease [7]. The presence of albuminuria (micro + macro) was significantly associated ($P \leq 0.04$) with definite and possible coronary heart disease within each of the three Strong Heart Study sites (Howard, manuscript submitted). The apparent clustering of complications with albuminuria has raised the possibility that albuminuria is simply a reflection of a more widespread vasculopathy affecting the heart, eyes and kidneys [36]. It cannot be determined from these cross sectional data whether the American Indians in the Strong Heart Study, in whom non-insulin-dependent (type 2) diabetes predominates, will follow a similar pattern of multi-organ deterioration found in whites with type 1 diabetes mellitus. However, evidence of progression from microalbuminuria to end-stage renal disease among non-Indian diabetic individuals should raise considerable concern. Furthermore, as shown by Neil and his colleagues, microalbuminuria (40 to 200 mg/liter) is also a significant independent predictor of mortality in those with diabetes during a mean follow-up period of 6.1 years [1], and among Pima Indians, the degree of albuminuria, even within the range classified as normal or microalbuminuria, predicts worsening to overt proteinuria [11], and nearly all the excess mortality associated with non-insulin dependent diabetes occurred in those with overt proteinuria [37].

In conclusion, there were significant differences in the prevalence of abnormal albuminuria between the three study sites, with the highest prevalence among participants in Arizona. While systolic hypertension and diabetes were clearly related to albuminuria, normotensive nondiabetic participants from Arizona were more likely to have abnormal albuminuria than similar participants from the other two sites. Indian heritage seemed to be directly related to the presence of albuminuria, suggesting a genetic susceptibility to renal disease. Further work is needed to define the genetic and or environmental factors that lead to renal impairment. This information may be helpful in coping with a potentially large and unfortunate disease burden falling on these Indian communities.

Acknowledgments

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